*REMARKS/ARGUMENTS*

*The Present Invention*

The present invention is directed to a method of preparing dual specificity lymphocytes.

*The Pending Claims*

Claims 41 and 94-109 are pending.

*The Final Office Action*

The Final Office Action maintains the rejection of claims 1, 8, 40, 41, 45, 46, 52, 56, 58, 61, 71, 79, 80, 83, 86, 87, and 92 as allegedly anticipated by Clay et al., *J. Immunology* 163: 507-513 (1999) (hereinafter Clay). Claims 1, 4, 7, 8, 10, 40, 41, 44, 45, 46, 52-61, 71, 72, 74-76, 79-87, and 89-93 are rejected under Section 103 as allegedly unpatentable in view of Hwu et al., *Cancer Res.* 55: 3369-3373 (1995) (hereinafter Hwu) and Munz et al., *J. Immunol.* 162: 25-34 (1999) (hereinafter Munz). Reconsideration of the rejections is hereby requested.

*The Amendments to the Claims*

Claims 1, 4, 7, 8, 10, 40, 44-46, 52-61, 71, 72, 74-76, 79-87, and 89-93 have been canceled. Claim 41 has been amended to recite "dual specificity lymphocytes" which is supported by the specification at, for example, paragraph [0042]. Claim 41 also has been amended to recite "one or more lymphocytes, thereby selecting for lymphocytes comprising an endogenous receptor reactive with the allogeneic cell" which is supported by the specification at, for example, lines 1-10 of paragraph [0053].

Claims 94-109 have been added herein. Claims 96-98, 100, 103, and 108 are essentially the same as previous claims 57, 59, 60, 61, 58, and 71, respectively. Claims 94 and 95 are supported by the specification at, for example, paragraphs [0064] and [0049], respectively. Claim 99 is supported by the specification at, for example, paragraphs [0055] and [0062]. Claim 101 is supported by the specification at, for example, paragraph [0089], and claim 102 is supported by the specification at, for example, paragraph [0039] and

Example 1. Claims 104-106 are supported by the specification at, for example, paragraphs [0089], [0058], and [0059], respectively, while claim 107 is supported by Example 12. No new matter has been added by way of these amendments.

*Discussion of the Anticipation Rejection*

The Final Office Action maintains that claims 1, 8, 40, 41, 45, 46, 52, 56, 58, 61, 71, 79, 80, 83, 86, 87, and 92 are anticipated by Clay, which allegedly discloses a composition comprising peripheral blood lymphocytes (PBL) transduced with a chimeric receptor reactive with the MART-1 tumor antigen and co-cultured with irradiated allogeneic PBMC and irradiated allogeneic EBV-B cells. This rejection is traversed for the reasons set forth below.

As a first matter, claims 1, 8, 40, 45, 46, 52, 56, 79, 80, 83, 86, 87, and 92 have been canceled. Thus, the rejection as it pertains to these claims is moot.

Clay discloses PBL transduced with genes encoding a MART-1-specific TCR. As pointed out in the previous Reply submitted on June 8, 2007, Clay discloses that the genes encoded the full-length alpha or beta chain of the MART-1 specific TCR. As such, Clay et al. does not disclose a T lymphocyte comprising a recombinant *chimeric* receptor. Since all of the instantly pending claims require that the lymphocytes are transduced with a *chimeric* receptor gene, Clay does not anticipate these claims.

The Final Office Action contends that the meaning of "chimeric" is "composed of parts of different origin" and concludes that Clay anticipates the claims, as the TCR of Clay is composed of at least two different parts. However, Clay teaches (at, for instance, the third sentence of the first complete paragraph of the right column on page 507, in combination with the second sentence of the second complete paragraph of the right column on page 507, and the paragraph entitled "Retroviral vector and supernatant production" on page 508) that the TCR of Clay is "derived from a TIL culture from patient 501." Accordingly, the parts of the TCR of Clay are not from different origins. Therefore, the TCR of Clay cannot be considered as "chimeric."

In view of the foregoing, Clay et al. does not anticipate the pending claims. Applicants therefore request the withdrawal of the rejection.

*Discussion of the Obviousness Rejection*

Claims 1, 4, 7, 8, 10, 40, 41, 44, 45, 46, 52-61, 71, 72, 74-76, 79-87, and 89-93 are rejected under Section 103 as allegedly unpatentable in view of Hwu and Munz. Specifically, the Final Office Action contends that Hwu teaches a composition comprising a T cell comprising a chimeric receptor, a syngeneic cell to which the T cell is reactive, and culture medium, which allegedly is a pharmaceutically acceptable carrier. According to the Final Office Action, Hwu does not teach the composition of the invention, because the composition of Hwu does not comprise an allogeneic cell to which the T cell is reactive.

The Final Office Action argues that Munz supplements the teachings of Hwu by establishing that using allogeneic cells as T cell stimulus is desirable for obtaining potent tumor reactive cytotoxic T lymphocytes. The Final Office Action concludes that one of ordinary skill in the art would have been motivated to modify the teachings of Hwu to arrive at the present invention to obtain the potent tumor reactive CTL of Munz.

The rejection is traversed, because the instantly pending claims are directed to a method of preparing dual specificity T cells and a composition comprising a population of cells comprising the lymphocytes produced by the inventive method and the allogeneic cell, wherein the method comprises contacting lymphocytes with a cell that is allogeneic to one or more lymphocytes, thereby selecting for lymphocytes comprising an endogenous receptor reactive with the allogeneic cell.

As a whole, Hwu teaches the transduction of genes encoding tumor reactive chimeric receptors into T cells and the use of such T cells for treating cancer. See, for example, the first sentence of the Discussion Section. However, Hwu does not teach or suggest T cells comprising a tumor reactive chimeric TCR *and* an alloreactive endogenous TCR. In fact, T cells comprising an *endogenous* TCR with a particular antigen specificity (e.g., specificity for an alloantigen) entails that such T cells are selected for, whereas Hwu teaches that the transduction of genes encoding chimeric TCRs into T cells eliminates the need to isolate naturally occurring T cells with a particular antigen specificity, i.e., with a particular native TCR. See, the first three sentences of the Discussion Section. Accordingly, Hwu teaches away from the concept of selecting for naturally occurring T cells with a particular antigen specificity, which is a feature of the methods and compositions claimed herein. In view of

the foregoing, one of ordinary skill in the art, after reading Hwu as a whole, would not have been motivated to select for naturally occurring alloreactive T cells and then transducing the T cells with tumor reactive chimeric TCR genes.

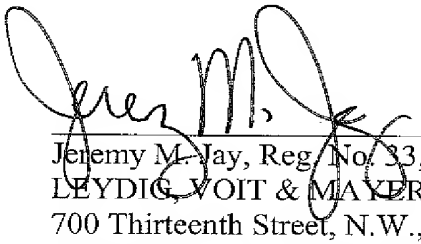
Munz teaches T cells comprising a single tumor reactive, alloreactive TCR. After reading Munz, one of ordinary skill in the art would not have been motivated to transduce T cells with a gene encoding a tumor reactive chimeric TCR. Therefore, Munz does not cure the deficiency of Hwu.

Accordingly, the instantly pending claims are patentable in view of Hwu and Munz. Applicants therefore request the withdrawal of the rejection under Section 103.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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